

~~17~~ 22. (Amended) An isolated [peptide] molecule comprising a polypeptide that induces an hepatitis C virus (HCV)-specific response in cytotoxic T lymphocytes having a sequence that [differs no more than about 20% from] has (a) no more than a total of two substitutions, deletions or insertions at the corresponding amino acid positions in a CTL epitope which is *Wait. sup?*
[ADLMGYIPLV (Core₁₃₁₋₁₄₀; SEQ ID NO:1), DLMGYIPLV (Core₁₃₂₋₁₄₀; SEQ ID NO:54),]
LLALLSCLTV (Core₁₇₈₋₁₈₇; SEQ ID NO:2), QLRRHIDLLV (E1₂₅₇₋₂₆₆; SEQ ID NO:3),
[LLCPAGHAV (NS3₁₁₆₉₋₁₁₇₇; SEQ ID NO:26),] KLVALGINAV (NS3₁₄₀₆₋₁₄₁₅; SEQ ID NO:28),
[SLMAFTAAV (NS4₁₇₈₉₋₁₇₉₇; SEQ ID NO:34),] or LLFNILGGWV (NS4₁₈₀₇₋₁₈₁₆; SEQ ID NO:35),
[or ILDSFDPLV (NS5₂₂₅₂₋₂₂₆₀; SEQ ID NO:42)] or

12 (b) has no more than one substitution, deletion or insertion at the corresponding amino acid positions as in a CTL epitope which is ADLMGYIPLV (Core₁₃₁₋₁₄₀; SEQ ID NO:1), DLMGYIPLV (Core₁₃₂₋₁₄₀; SEQ ID NO:54), LLCPAGHAV (NS3₁₁₆₉₋₁₁₇₇; SEQ ID NO:26), SLMAFTAAV (NS4₁₇₈₉₋₁₇₉₇; SEQ ID NO:34), or ILDSFDPLV (NS5₂₂₅₂₋₂₂₆₀; SEQ ID NO:42),
wherein said molecule comprises at least eight amino acids and less than 50 amino acids, with the proviso that when said selected CTL epitope is SLMAFTAAV (NS4₁₇₈₉₋₁₇₉₇; SEQ ID NO:34), then said molecule comprises from at least eight amino acids to less than 25 amino acids, when said polypeptide is LLALLSCLTV (Core₁₇₈₋₁₈₇; SEQ ID NO:2) then said molecule comprises at most ten amino acids, and when said polypeptide is DLMGYIPLV (Core₁₃₂₋₁₄₀; SEQ ID NO:54), then said molecule comprises at most nine amino acids.

23. (Amended) The [isolated peptide] molecule of claim 22, wherein the isolated peptide has less than 20 amino acids.

24. (Amended) The [isolated peptide] molecule of claim 22, wherein the isolated peptide has from 8 to 12 amino acids.

25. (Amended) The [isolated peptide] molecule of claim 22, wherein the isolated peptide has 9 or 10 amino acids.

Please cancel claims 26-29 without prejudice or disclaimer..

C3 30. (Amended) The [isolated peptide] molecule of claim 22, 23, 24, or 25, wherein the isolated [peptide] molecule has [the] a sequence that [differs no more than about 20% from] has no more than a total of one amino acid substitution, deletion or insertion at the corresponding position as in LLALLSCLTV (Core₁₇₈₋₁₈₇; SEQ ID NO:2).

Please cancel claim 31 without prejudice or disclaimer.

C4 32. (Amended) The [isolated peptide] molecule of claim 22, 23, 24, or 25, wherein the isolated [peptide] molecule has [the] a sequence that [differs no more than about 20% from] has no more than a total of one amino acid substitution, deletion or insertion at the corresponding position as in QLRRHIDLLV (E1₂₅₇₋₂₆₆; SEQ ID NO:3).

Please cancel claims 33-35 without prejudice or disclaimer.

C5 36. (Amended) The [isolated peptide] molecule of claim 22, 23, 24, or 25, wherein the isolated [peptide] molecule has [the] a sequence that [differs no more than about 20% from] has no more than a total of one amino acid substitution, deletion or insertion at the corresponding position as in KLVALGINAV (NS3₁₄₀₆₋₁₄₁₅; SEQ ID NO:28).

Please cancel claims 37-39 without prejudice or disclaimer.

C6 40. (Amended) The [isolated peptide] molecule of claim 22, 23, 24, or 25, wherein the isolated [peptide] molecule has [the] a sequence that [differs no more than about 20% from] has no more than a total of one amino acid substitution, deletion or insertion at the corresponding position as in LLFNILOGGWV (NS4₁₈₀₇₋₁₈₁₆; SEQ ID NO:35).

Please cancel claims 41-43 without prejudice or disclaimer.

C7 44. (Amended) An immunogenic composition that induces an hepatitis C virus (HCV)-specific response in cytotoxic T lymphocytes (CTL) comprising molecule which comprises a peptide having a sequence that [differs no more than about 20% from] has no more than a total of a total of two amino acid substitutions, deletions or insertions at the corresponding positions as in a CTL epitope which is ADLMGYIPLV (Core₁₃₁₋₁₄₀; SEQ ID

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NO:1), [DLMGYIPLV (Core₁₃₂₋₁₄₀; SEQ ID NO:54),] LLALLSCLTV (Core₁₇₈₋₁₈₇; SEQ ID NO:2), QLRRHIDLLV (E1₂₅₇₋₂₆₆; SEQ ID NO:3), [LLCPAGHAV (NS3₁₁₆₉₋₁₁₇₇; SEQ ID NO:26),] KLVALGINAV (NS3₁₄₀₆₋₁₄₁₅; SEQ ID NO:28), [SLMAFTAAV (NS4₁₇₈₉₋₁₇₉₇; SEQ ID NO:34),] or LLFNILGGWV (NS4₁₈₀₇₋₁₈₁₆; SEQ ID NO:35) or

has no more than a total of one substitution, deletion or insertion at the corresponding amino acid positions as in a CTL epitope which is DLMGYIPLV (Core₁₃₂₋₁₄₀; SEQ ID NO:54), LLCPAGHAV (NS3₁₁₆₉₋₁₁₇₇; SEQ ID NO:26), SLMAFTAAV (NS4₁₇₈₉₋₁₇₉₇; SEQ ID NO:34), or ILDSFDPLV (NS5₂₂₅₂₋₂₂₆₀; SEQ ID NO:42).

45. The immunogenic composition of claim 44, wherein the immunogenic composition further comprises a label selected from the group consisting of a radioactive label, an enzymatic label, and a fluorescent label.

46. The immunogenic composition of claim 44, wherein the immunogenic composition further comprises a solid matrix.

47. The immunogenic composition of claim 44, wherein the immunogenic composition further comprises a carrier molecule.

48. The immunogenic composition of claim 44, wherein the carrier molecule comprises a protein or an immunogenic lipid.

49. The immunogenic composition of claim 44, wherein the immunogenic composition further comprises a T-helper lymphocyte epitope.

50. The immunogenic composition of claim 44, wherein the immunogenic composition further comprises an additional peptide.

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51. (Amended) The immunogenic composition of claim [44] 50, wherein the additional peptide has a sequence that [differs no more than about 20% from] has no more than a total of two amino acid substitutions, deletions or insertions at the corresponding positions as in KLVALGINAV (NS3₁₄₀₆₋₁₄₁₅; SEQ ID NO:28).

52. (Amended) A method of stimulating a cytotoxic T-lymphocyte (CTL) response to an hepatitis C viral immunogen, comprising contacting an HLA class I-restricted cytotoxic T lymphocyte with a composition comprising a peptide that induces an hepatitis C virus (HCV)-specific response in cytotoxic T lymphocytes having [the] a sequence that [differs no more than about 20% from] has no more than a total of two amino acid substitutions, deletions or insertions at the corresponding positions as in a CTL epitope which is ADLMGYIPLV (Core₁₃₁₋₁₄₀; SEQ ID NO:1), [DLMGYIPLV (Core₁₃₂₋₁₄₀; SEQ ID NO:54),] LLALLSCLTV (Core₁₇₈₋₁₈₇; SEQ ID NO:2), QLRRHIDLLV (E1₂₅₇₋₂₆₆; SEQ ID NO: 3), [LLCPAGHAV (NS3₁₁₆₉₋₁₁₇₇; SEQ ID NO:26),] KLVALGINAV (NS3₁₄₀₆₋₁₄₁₅; SEQ ID NO:28), [SLMAFTAAV (NS4₁₇₈₉₋₁₇₉₇; SEQ ID NO:34),] or LLFNILGGWV (NS4₁₈₀₇₋₁₈₁₆; SEQ ID NO:35) or
has no more than a total of one substitution, deletion or insertion at the corresponding amino acid positions as in a CTL epitope which is ADLMGYIPLV (Core₁₃₁₋₁₄₀; SEQ ID NO:1), DLMGYIPLV (Core₁₃₂₋₁₄₀; SEQ ID NO:54), LLCPAGHAV (NS3₁₁₆₉₋₁₁₇₇; SEQ ID NO:26), SLMAFTAAV (NS4₁₇₈₉₋₁₇₉₇; SEQ ID NO:34), or ILDSFDPLV (NS5₂₂₅₂₋₂₂₆₀; SEQ ID NO:42).

53. The method of claim 52, wherein the contacting occurs in a mammal.

54. The method of claim 52, wherein the mammal is free of HCV disease, is a carrier of HCV, or is afflicted with HCV disease.

55. The method of claim 52, wherein the contacting occurs *in vitro*.

56. A method of detecting cytotoxic T cells that respond to a T cell epitope of hepatitis C virus (HCV), the method comprising the steps of: (a) preparing HLA class I-restricted cytotoxic T cells; (b) preparing HLA class-I matched and -mismatched target cells; (c) containing separately matched and mismatched target cells with a composition comprising a peptide that induces an HCV-specific response in cytotoxic T lymphocytes having the sequence that [differs no more than about 20% from] has no more than a total of two amino acid substitutions, deletions or insertions at the corresponding positions as in a CTL epitope which is
ADLMGYIPLV (Core₁₃₁₋₁₄₀; SEQ ID NO:1), [DLMGYIPLV (Core₁₃₂₋₁₄₀; SEQ ID NO:54),] LLALLSCLTV (Core₁₇₈₋₁₈₇; SEQ ID NO:2), QLRRHIDLLV (E1₂₅₇₋₂₆₆; SEQ ID NO: 3),

[LLCPAGHAV (NS3₁₁₆₉₋₁₁₇₇; SEQ ID NO:26),] KLVALGINAV (NS3₁₄₀₆₋₁₄₁₅; SEQ ID NO:28), [SLMAFTAAV (NS4₁₇₈₉₋₁₇₉₇; SEQ ID NO:34),] or LLFNILGGWV (NS4₁₈₀₇₋₁₈₁₆; SEQ ID NO:35) or has no more than a total of one substitution, deletion or insertion at the corresponding amino acid positions as in a CTL epitope which is DLMGYIPLV (Core₁₃₂₋₁₄₀; SEQ ID NO:54), LLCPAGHAV (NS3₁₁₆₉₋₁₁₇₇; SEQ ID NO:26), SLMAFTAAV (NS4₁₇₈₉₋₁₇₉₇; SEQ ID NO:34), or ILDSFDPLV (NS5₂₂₅₂₋₂₂₆₀; SEQ ID NO:42); (d) combining the cytotoxic T cells separately with the matched and mismatched target cells; and (e) measuring cytotoxicity.

57. The method of claim 56, wherein the cytotoxic T cells are combined with HLA class I-matched lymphocytes.

58. (Amended) A pharmaceutical composition comprising a peptide that induces an hepatitis C virus (HCV)-specific response in cytotoxic T lymphocytes having a sequence that [differs no more than about 20% from] has no more than a total of two amino acid substitutions, deletions or insertions at the corresponding positions as in a CTL epitope which is ADLMGYIPLV (Core₁₃₁₋₁₄₀; SEQ ID NO:1), [DLMGYIPLV (Core₁₃₂₋₁₄₀; SEQ ID NO:54),] LLALLSCLTV (Core₁₇₈₋₁₈₇; SEQ ID NO:2), QLRRHIDLLV (E1₂₅₇₋₂₆₆; SEQ ID NO: 3), [LLCPAGHAV (NS3₁₁₆₉₋₁₁₇₇; SEQ ID NO:26),] KLVALGINAV (NS3₁₄₀₆₋₁₄₁₅; SEQ ID NO:28), [SLMAFTAAV (NS4₁₇₈₉₋₁₇₉₇; SEQ ID NO:34),] or LLFNILGGWV (NS4₁₈₀₇₋₁₈₁₆; SEQ ID NO:35) or has no more than a total of one substitution, deletion or insertion at the corresponding amino acid positions as in a CTL epitope which is DLMGYIPLV (Core₁₃₂₋₁₄₀; SEQ ID NO:54), LLCPAGHAV (NS3₁₁₆₉₋₁₁₇₇; SEQ ID NO:26), SLMAFTAAV (NS4₁₇₈₉₋₁₇₉₇; SEQ ID NO:34), or or ILDSFDPLV (NS5₂₂₅₂₋₂₂₆₀; SEQ ID NO:42), and a pharmaceutically acceptable carrier.

59. The pharmaceutical composition of claim 58, wherein the peptide has less than 20 amino acids.

Please enter the following new claims:

60. (New) A conjugate comprising
(a) a molecule, which comprises:

a polypeptide an having no more than a total of two amino acid substitutions, deletions or insertions at the corresponding positions as in a

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CTL epitope which is ADLMGYIPLV (Core₁₃₁₋₁₄₀; SEQ ID NO:1),
LLALLSCLTV (Core₁₇₈₋₁₈₇; SEQ ID NO:2), QLRRHIDLLV (E1₂₅₇₋₂₆₆;
SEQ ID NO: 3), KLVALGINAV (NS3₁₄₀₆₋₁₄₁₅; SEQ ID NO:28),
LLFNILGGWV (NS4₁₈₀₇₋₁₈₁₆; SEQ ID NO:35) or has no more than a total
of one substitution, deletion or insertion at the corresponding amino acid
positions as in a CTL epitope which is DLMGYIPLV (Core₁₃₂₋₁₄₀; SEQ ID
NO:54), LLCPAGHAV (NS3₁₁₆₉₋₁₁₇₇; SEQ ID NO:26), SLMAFTAAV
(NS4₁₇₈₉₋₁₇₉₇; SEQ ID NO:34), or or ILDSFDPLV (NS5₂₂₅₂₋₂₂₆₀; SEQ ID
NO:42),; and

(b) a substance selected from the group consisting of a radiolabel, an enzyme, a
fluorescent label, a solid matrix, a carrier and an additional molecule of (a).

-- 61. (New) The conjugate of claim 60, wherein said carrier comprises an
immunogenic lipid or protein.

~~62.~~ 62. (New) A conjugate of claim 60 comprising two molecules, each comprising:
a polypeptide no more than a total of two amino acid substitutions, deletions or
insertions at the corresponding positions as in a CTL epitope which is ADLMGYIPLV (Core₁₃₁₋₁₄₀;
SEQ ID NO:1), LLALLSCLTV (Core₁₇₈₋₁₈₇; SEQ ID NO:2), QLRRHIDLLV (E1₂₅₇₋₂₆₆; SEQ
ID NO: 3), KLVALGINAV (NS3₁₄₀₆₋₁₄₁₅; SEQ ID NO:28), LLFNILGGWV (NS4₁₈₀₇₋₁₈₁₆; SEQ ID
NO:35) or has no more than a total of one substitution, deletion or insertion at the corresponding
amino acid positions as in a CTL epitope which is DLMGYIPLV (Core₁₃₂₋₁₄₀; SEQ ID NO:54),
LLCPAGHAV (NS3₁₁₆₉₋₁₁₇₇; SEQ ID NO:26), SLMAFTAAV (NS4₁₇₈₉₋₁₇₉₇; SEQ ID NO:34), or or
ILDSFDPLV (NS5₂₂₅₂₋₂₂₆₀; SEQ ID NO:42),.

-- 63. (New) The conjugate of claim 62, wherein at least one of said molecules
comprises at least eight amino acids and less than 50 amino acids.

-- 64. (New) The conjugate of claim 62, further comprising a T helper epitope. --

REMARKS